

What is claimed is:

- 5 1. A method for preventing or treating an inflammation-related disorder in a subject in need thereof, which method comprises treating the subject with a therapeutically effective amount of an aldosterone blocker or pharmaceutically-acceptable salts thereof.
- 10 2 The method of Claim 1 wherein said inflammation-related disorder is selected from the group consisting of trauma-induced inflammation, surgically-induced inflammation, bacterial-induced inflammation and viral induced inflammation.
- 15 3. The method of Claim 1 wherein the inflammation-related disorder is a cardiovascular disorder.
4. The method of Claim 3 wherein said said cardiovascular disorder is selected from the group consisting of: coronary artery disease; aneurysm; arteriosclerosis; atherosclerosis; myocardial infarction; embolism; stroke; 20 thrombosis; angina; vascular plaque inflammation; vascular plaque rupture; Kawasaki disease; calcification; and inflammation.
5. The method of Claim 4 wherein said calcification is selected from the 25 group consisting of vascular calcification and valvar calcification.
6. The method of Claim 3 wherein the cardiovascular disorder is atherosclerosis.
- 30 7. The method of Claim 3 wherein the cardiovascular disorder is thrombosis.
8. The method of Claim 3 wherein the cardiovascular disorder occurs, in whole or in part, in the kidney.

9. The method of Claim 3 wherein the cardiovascular disorder occurs, in whole or in part, in the brain.

5 10. The method of Claim 3 wherein the cardiovascular disorder occurs, in whole or in part, in the heart.

11. The method of Claim 1 wherein said aldosterone blocker is an aldosterone receptor antagonist.

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12. The method of Claim 11 wherein said aldosterone receptor antagonist is a spirolactone-type compound.

13. The method of claim 11 wherein said spirolactone-type compound is
15 selected from the group consisting of 7α -acetylthio-3-oxo-4,15-androstadiene-[17(β -1')-spiro-5']perhydrofuran-2'-one;

3-oxo- 7α -propionylthio-4,15-androstadiene-[17((β -1')-spiro-5')perhydrofuran-2'-one;

6 β ,7 β -methylene-3-oxo-4,15-androstadiene-[17((β -1')-spiro-5')perhydrofuran-2'-one;

20 15 α ,16 α -methylene-3-oxo-4, 7α -propionylthio-4-androstene[17(β -1')-spiro-5']perhydrofuran-2'-one;

6 β ,7 β ,15 α ,16 α -dimethylene-3-oxo-4-androstene[17(β -1')-spiro-5']perhydrofuran-2'-one;

25 7α -acetylthio-15 β ,16 β -Methylene-3-oxo-4-androstene-[17(β -1')-spiro-5']perhydrofuran-2'-one;

15 β ,16 β -methylene-3-oxo- 7β -propionylthio-4-androstene-[17(β -1')-spiro-5']perhydrofuran-2'-one; and

6 β ,7 β ,15 β ,16 β -dimethylene-3-oxo-4-androstene-[17(β -1')-spiro-5']perhydrofuran-2'-one.

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14. The method of Claim 11 wherein said aldosterone receptor antagonist is spironolactone.

15. The method of Claim 11 wherein said aldosterone receptor antagonist is
5 an epoxy-steroidal aldosterone antagonist.

16. The method of Claim 15 wherein said epoxy-steroidal compound has an epoxy moiety fused to the "C" ring of the steroidal nucleus of a 20-spiroxane compound.

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17. The method of Claim 15 wherein said 20-spiroxane compound is characterized by the presence of a 9-alpha,11-beta-substituted epoxy moiety.

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18. The method of Claim 15 wherein said epoxy-steroidal compound is selected from the group consisting of:

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, methyl ester, (7 α ,11 α ,17 β)-;

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Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-dimethyl ester, (7 α ,11 α , 17 β)-;

3'H-cyclopropa[6,7] pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, γ -lactone, (6 β ,7 β ,11 α ,17 β)-;

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo, 7-(1-methylethyl) ester, monopotassium salt, (7 α ,11 α ,17 β)-;

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Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, 7-methyl ester, monopotassium salt, (7 α ,11 α ,17 β)-;

3'H-cyclopropa[6,7]pregna-1,4,6-triene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, γ -lactone, (6 β ,7 β ,11 α ,)-;

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3'H-cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, methyl ester, (6 β ,7 β ,11 α ,17 β)-;

3'H-cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, monopotassium salt, (6 β ,7 β ,11 α ,17 β)-;

5 3'H-cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, γ -lactone, (6 β ,7 β ,11 α ,17 β)-;

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, ethyl ester, (7 α ,11 α ,17 β)-;and

Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, 1-methylethyl ester, ((7 α ,11 α ,17 β))-.

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19. The method of Claim 11 wherein said aldosterone receptor antagonist is epoxymexrenone.

20. The method of claim 11 wherein said aldosterone receptor antagonist is
15 Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-dimethyl ester, (7 α ,11 α , 17 β)-.

21. The method of claim 11 wherein said aldosterone receptor antagonist is
20 3'H-cyclopropa[6,7] pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, γ -lactone, (6 β ,7 β ,11 α ,17 β)-.

22. The method of claim 11 wherein said aldosterone receptor antagonist is Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo, 7-(1-methylethyl) ester, monopotassium salt, (7 α ,11 α ,17 β)-.

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23. The method of claim 11 wherein said aldosterone receptor antagonist is Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, 7-methyl ester, monopotassium salt, (7 α ,11 α ,17 β)-.

30 24. The method of claim 11 wherein said aldosterone receptor antagonist is 3'H-cyclopropa[6,7]pregna-1,4,6-triene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, γ -lactone, (6 β ,7 β ,11 α ,-).

25. The method of claim 11 wherein said aldosterone receptor antagonist is 3'H-cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, methyl ester, (6 β ,7 β ,11 α ,17 β)-.

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26. The method of claim 11 wherein said aldosterone receptor antagonist is 3'H-cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, monopotassium salt, (6 β ,7 β ,11 α ,17 β)-.

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27. The method of claim 11 wherein said aldosterone receptor antagonist is 3'H-cyclopropa[6,7]pregna-4,6-diene-21-carboxylic acid, 9,11-epoxy-6,7-dihydro-17-hydroxy-3-oxo-, γ -lactone, (6 β ,7 β ,11 α ,17 β)-.

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28. The method of claim 11 wherein said aldosterone receptor antagonist is Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, ethyl ester, (7 α ,11 α ,17 β)-.

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29. The method of claim 11 wherein said Aldosterone receptor antagonist is Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ -lactone, ethyl ester, (7 α ,11 α ,17 β)-.

30. The method of claim 11 wherein said aldosterone receptor antagonist is drospirenone.

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31. The method of Claim 15 wherein the amount of epoxy-steroidal compound administered is between about 0.5 mg to about 500 mg per day

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32. The method of Claim 15 wherein the therapeutically-effective amount of epoxy-steroidal compound administered is between about 0.5 mg to about 100 mg per day.

33. The method of Claim 15 wherein the therapeutically-effective amount of

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epoxy-steroidal compound administered is between about 10 mg to about 100 mg per day.

5 34. The method of Claim 15 wherein the therapeutically-effective amount of epoxy-steroidal compound administered is between about 0.5 mg to about 25 mg per day.

10 35. The method of Claim 15 wherein the therapeutically-effective amount of epoxy-steroidal compound administered is between about 0.5 to about 10 mg per day.

15 36. The method of Claim 1 wherein said aldosterone blocker is 11 β -Hydroxy androst-4-en-3-one 17-spirolactone, or a pharmaceutically acceptable salt thereof.

 37. The method of claim 1 wherein said aldosterone blocker is an aldosterone inhibitor.

20 38. The method of Claim 37 wherein said aldosterone inhibitor is selected from the group consisting of: Aromatase inhibitors; 12-Lipoxygenase inhibitors; P450_{11 β} inhibitors; Atrial natriuretic factors; 20 Lysase inhibitors; PKC inhibitors; Benzodiazepines; Calcium blockers; Diacylglycerol lipase inhibitors; Potassium ionophores, Electron transport blockers; and ethanol, or a pharmaceutically
25 acceptable salt thereof.

 39. The method of Claim 37 wherein said aldosterone inhibitor is a diacylglycerol lipase inhibitor.

30 40. The method of Claim 39 wherein said diacylglycerol lipase inhibitor is 1,6-bis- cyclohexyloximinocarbonylamino)-hexane, or a pharmaceutically acceptable salt thereof.

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44. The method of Claim 43 wherein said aromatase inhibitor is fadrozole, or a pharmaceutically acceptable salt thereof.

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45. The method of Claim 37 wherein said aldosterone inhibitor is a lipoyxygenase inhibitor.

46. The method of Claim 45 wherein said Lipxygenase inhibitor is phenidone, or a pharmaceutically acceptable salt thereof.

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47. The method of Claim 37 wherein said aldosterone inhibitor is a P450_{11β} inhibitor.

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48. The method of Claim 47 wherein said P450_{11β} inhibitor is 18-vinylprogesterone, or a pharmaceutically acceptable salt thereof.

49. The method of Claim 1 wherein said aldosterone blocker is an aldosterone synthase inhibitor.

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50. A method of preventing or treating an inflammation-related disorder in a subject, said method comprising treating the subject with a therapeutically-effective amount of an aldosterone blocker sufficient to alter the expression of one or more expression products involved, directly or indirectly, in the regulation of

inflammation in the subject.

51. The method of Claim 50 wherein said inflammation-related disorder occurs in a tissue of said subject.

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52. The method of Claim 50 wherein said inflammation-related disorder occurs in an organ of said subject.

53. The method of Claim 52 wherein said organ is the heart.

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54. The method of Claim 52 wherein said organ is the brain.

55. The method of Claim 52 wherein said organ is the kidney.

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56. The method of Claim 50 wherein the increased expression of one or more of said expression products is involved, directly or indirectly, in the regulation of inflammation in the subject.

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57. The method of Claim 50 wherein the decreased expression of one or more of said expression products is involved, directly or indirectly, in the regulation of inflammation in the subject.

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58. The method of Claim 50 wherein two or more of said expression products are co-expressed simultaneously.

59. The method of Claim 50 wherein three or more of said expression products are co-expressed sequentially.

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60. The method of Claim 50 wherein said expression products are selected from the group consisting of cyclooxygenase-2, osteopontin, MCP-1, ICAM-1, VCAM-1, ANF, $\alpha_v\beta_3$, Inf- γ , IL-1, TNF- α , NADH/NADPH oxidase, superoxide free radicals, TXA2, b-FGF, CD44, endothelin, Angiotensin II receptor, active t-PA, inactive t-PA, PAI-1, CRP, IL-6, IL-10, IL-12, Troponin T, HSP65, amyloid,

Phospholipase A2, fibrinogen, CD40/CD40L, collagen binding integrin $\alpha 1\beta 1$ and collagen binding integrin $\alpha 2\beta 1$.

61. The method of Claim 50 wherein said expression products are selected
5 from the group consisting of cyclooxygenase-2, osteopontin, MCP-1, ICAM-1, VCAM-1, ANF, $\alpha_v\beta_3$, Inf- γ , IL-1, TNF- α , NADH/NADPH oxidase, superoxide free radicals, TXA2, b-FGF, CD44, endothelin, Angiotensin II receptor, active t-PA, inactive t-PA and PAI-1.

10 62. The method of Claim 50 wherein said expression product comprises cyclooxygenase-2.

63. The method of Claim 62 wherein said cyclooxygenase-2 is co-expressed
15 with one or more expression products selected from the group consisting of osteopontin, MCP-1, ICAM-1 and VCAM-1.

64. The method of Claim 50 wherein said expression product comprises osteopontin.

20 65. The method of Claim 64 wherein said osteopontin is co-expressed with one or more expression products selected from the group consisting of cyclooxygenase-2, MCP-1, ICAM-1 and VCAM-1.

25 66. The method of Claim 50 wherein said expression product comprises MCP-1.

67. The method of Claim 64 wherein said MCP-1 is co-expressed with one
or more expression products selected from the group consisting of cyclooxygenase-2, osteopontin, ICAM-1 and VCAM-1.

30 68. The method of Claim 50 wherein said expression product comprises ICAM-1.

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69. The method of Claim 68 wherein said ICAM-1 is co-expressed with one or more expression products selected from the group consisting of cyclooxygenase-2, osteopontin, MCP-1 and VCAM-1.

70. The method of Claim 50 wherein said expression product comprises VCAM-1.

71. The method of Claim 70 wherein said VCAM-1 is co-expressed with
one or more expression products selected from the group consisting of
10 cyclooxygenase-2, osteopontin, ICAM-1 and MCP-1.